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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,493	07/18/2000	Jack Wands	MGH-0026	3498

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EXAMINER	
SHUKLA, RAM R	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/600,493	WANDS ET AL.	
	Examiner	Art Unit	
	Ram R. Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,6-8,17,20-28,34 and 36-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4, 6, 7, 8, 17, 20-28, 34, and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment and response filed 6-30-03 have been received and entered.

2. Claims 4, 6, 7, 8, 17, 20-28, 34, and 36-38 are under consideration.

In view of applicants' arguments, the 102 rejection of claims 4, 6, 8, 17, 34, 36 and 38 has been withdrawn.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 4, 6, 7, 8, 17, 20-28, 34, and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maertens et al (Maertens et al. WO 96/13590, 9 May 1996) or Maertens et al (Maertens et al. US 2002/0183508 A1, December 5, 2002) or Selby et al (J. Gen.Virol. 74:1103-1113, 1993) or Donnelly et al (WO 97/47358, 18 December, 1997) in view of Liao et al (WO 96/38474, 12 December 1996), Tokushige et al Hepatology 24:14-20, 1996) and Ferrari et al (Hepatology 19:286-295).

Maertens et al (WO document) teaches a recombinant expression vector comprising a polynucleotide comprising sequences that express NS4, NS5 and also comprise 5' UTR of hepatitis C virus (see the entire document, particularly, see claims 7, 8, 28, 29 and pages 15, 23, 25, 32-33, 41, 43-44). The vector comprises control elements for expression in eukaryotic cells as discussed in the specification.

Maertens et al (US Pre-grant publication) teaches a recombinant expression vector comprising a polynucleotide comprising sequences that express NS4, NS5 and also comprise 5' UTR of hepatitis C virus (see the entire document, particularly, see claims 7, 8, 26-29 and paragraphs 0051, 0130, 0217, 0241, 0286). The vector comprises control elements for expression in eukaryotic cells as discussed in the specification. These arts by Maertens et al do not teach a method of producing an immune response in an animal by administering a nucleic acid comprising a nucleic acid encoding a hepatitis C virus nonstructural protein or combination.

Selby et al teaches several constructs for expression of viral proteins. For example, the plasmid pHCV comprises the entire viral genome (see the methods section on page 1103, right column continued into the left column on page 1104 and figure 1). The plasmids pHCV5-1 and pHCV comprise the entire 5'UTR and 3'UTR and the coding sequence for the non-structural proteins. Since the protein of the virus is produced as a polyprotein, a fusion of NS4-NS5 would be produced as a result of partial proteolytic digestion.

Donnelly et al teach synthetic hepatitis C genes, pharmaceutical compositions and formulation for vaccination and gene therapy and method of immunization (see the entire document). Particularly the art teaches DNA constructs that encode hepatitis C NS5 gene or any other HCV gene that generates specific immune responses in animal s(see 17-31 on page 3, figures 12 and 13, page 13-20, lines 12-17 page 20, claims 1, 8-23, 25-26).

Liao et al teaches diagnosis of and vaccination against hepatitis c virus. The art teaches compositions and methods for the induction of immune responses in and vaccination of an animal. The art further teaches that combining unprocesses core region with a non-structural protein (such as an NS5 protein or an unprocesses NS3-NS4 fusion protein from HCV) results in a synergistic effect that greatly

enhances the already improved sensitivity and specificity provided by the unprocessed core region (see page 13, lines 21-25; page 18, lines 10-20). The art also teaches expression vectors that comprise a cDNA encoding NS5 nonstructural region.

Tokushige et al teaches a method of producing immune response to hepatitis c virus core protein using a DNA based vaccine construct. The construct comprises a CMV promoter, an RSV enhancer, 5' UTR of hepatitis c virus and the coding sequence for core protein. The art also teaches method of injecting the construct in a muscle and using bupivacaine (see the materials and methods section).

Ferrari et al teach T cell response to structural and non-structural hepatitis c virus antigens in persistent and self-limited hepatitis c virus infections. The art teaches that the core protein followed by the NS4 were the most potent T-cell immunogen for both chronic as well as asymptomatic anti-HCV-positive patients . The art also teaches that another paper taught that NS4 was the most immunogenic. The art also discusses role of other non-structural protein NS5.

Diepolder et al teach T cell response to the other non-structural hepatitis c protein N3 and note that TH0/TH1-like CD4T-lymphocyte response to NS3 and other nonstructural HCV proteins contributes to successful viral clearance, whereas the PBMC response to core protein may be more common in patients that develop chronic hepatitis C. They go on to suggest that NS3-specific CD4 T-cell response might be a candidate as a target for immunointervention in the treatment of acute, protracted and chronic hepatitis and for vaccine development.

At the time of the invention, it would have been obvious to an artisan of ordinary skill to modify the polynucleotides of Maertens et al, Selby et al or Donnely et al by cloning the non-structural protein encoding sequences as a fusion of HCV core protein in the vector of Tokushige et al or Donnelly et al to produce vectors that express HCV non-structural proteins alone or chimeric proteins and administer them to an animal and produce immune response with a reasonable expectation of success. An artisan of skill would have been motivated to produce vectors that encode non-structural proteins as a fusion with core protein because such as fusion protein was more immunogenic and use such for vaccination. It is noted that non-

structural proteins were known in the art to be strongly immunogenic and fusion of NS-5 or ns3-NS4 was found to be even more immunogenic by Liao et al. The art of record suggested their potential use in developing vaccine and treatment and also because fusion proteins, such as core followed by NS-4 were most potent immunogens.

Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection.

5. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (571) 272-0735 . The examiner can normally be reached on Monday through Friday

from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (571) 272-0548.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ram R. Shukla, Ph.D.
Primary Examiner
Art Unit 1632

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER